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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

Application Number	09/471,703
Filing Date	December 23, 1999
First Named Inventor	MERENKOVA, IRENA N.
Group Art Unit	1634
Examiner Name	SOUAYA, JEHANNE E
Attorney Docket Number	TGEN-001

ENCLOSURES (check all that apply)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment / Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Documents
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Assignment Papers *(for an Application)*
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s
- ☐ After Allowance Communication to Group
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- ☐ Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- ☐ Proprietary Information
- ☐ Status Letter
- ☒ Other Enclosure(s) *(please identify below):*
  1) **Petition for Certificate of Correction (2 pgs.)**
  2) **Certificate of Correction (1 pg.)**
  3) **Copy of Last Page of Issued Patent (1 pg.)**
  4) **Copy of Amendment as filed on July 2, 2003 (12 pgs.)**
  5) **Return Postcard**

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Signing Attorney/Agent (Reg. No.)	**EDWARD J. BABA (REG. NO. 52,581)** **BOZICEVIC, FIELD & FRANCIS LLP**
Signature	
Date	**August 6, 2004**

Certificate
AUG 12 2004
of Correction

EXPRESS MAIL LABEL NO. EV462737661US

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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17 AUG 2004

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PETITION FOR CERTIFICATE OF CORRECTION UNDER 37 C.F.R. § 1.322 FOR PATENT AND TRADEMARK OFFICE ERROR Address to: Assistant Commissioner for Patents Washington, D.C. 20231	Attorney Docket Number	TGEN-001
	First Named Inventor	IRENA N. MERENKOVA
	Application Number	09/471,703
	Filing Date	December 23, 1999
	Patent Number	6,762,018 B1
	Issue Date	July 13, 2004
	Title	ANALYSIS OF NUCLEOTIDE POLYMORPHISMS AT A SITE

Sir:

Applicants petition under 37 C.F.R. § 1.322 for a Certificate of Correction to correct errors in the claims for the above-identified patent due to Patent and Trademark Office error.

Transmitted herewith for filing is a Certificate of Correction for the above-identified patent. Please make the following corrections to Claims 1 and 5.

In Claim 1, column 13, line 24, please replace the word "provide" after the word "rNTPs" and before the word "for" with the word -- provides --.

In Claim 5, column 13, line 52, please remove the word -- primer -- after the word "analyzing" and before the word "comprises".

Enclosed is a copy of the Amendment and Response filed on July 2, 2003, showing the correct form of the Claims. Also enclosed, is a copy of the last page of the issued patent showing the incorrect language of the claims that resulted from Patent and Trademark Office error.

It is believed that no fee is due since the error was made by the Patent and Trademark Office. However, the Commissioner is hereby authorized to charge any fees under 37 C.F.R. § 1.20 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: August 6, 2004

By: _____
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Registration No. 52,581

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,762018 B1
DATED : July 13, 2004
INVENTOR(S) : Irena N. Merenkova

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

In Claim 1, column 13, line 24, the word "provide" should be -- provides --.

In Claim 5, column 13, line 52, the word -- primer -- after the word "analyzing" and before the word "comprises" should be removed.

MAILING ADDRESS OF SENDER:

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PATENT NO: 6,762,018 B1

No. of add'l copies
@ 50¢ per page

17 AUG 2004

-continued

<223> OTHER INFORMATION: Oligonucleotide

<400> SEQUENCE: 8

taatacgact cactataggg 20

What is claimed is:

1. A method for determining the identity of a polymorphic nucleotide in a target sequence having at least two known variant nucleotides at a site, comprising:

performing a primer extension reaction with the target sequence using an extension reaction mixture comprising:

a primer that specifically hybridizes to the target sequence such that there is a one or more nucleotide gap between the 3' terminus of the primer and the variant nucleotide of the polymorphic site of the target sequence, and

a mixture of deoxyribonucleoside triphosphates (dNTPs) or ribonucleoside triphosphates (rNTPs), where the mixture of dNTPs or rNTPs provide for at least one nucleotide extension of the primer when hybridized to a target sequence having either of the two variant nucleotides at the polymorphic site, wherein the mixture excludes a dNTP or rNTP complementary to one of said variant nucleotides of the polymorphic site, and wherein the dNTPs or rNTPs in the mixture are not detectably labeled or modified, and wherein the extension reaction is performed in the absence of a dideoxynucleoside triphosphate (ddNTP); and

analyzing primer extension products of said extension reaction;

wherein the length of the primer extension products is indicative of the identity of the variant nucleotides at the polymorphic site.

2. The method of claim 1, wherein the primer hybridizes to the target sequence such that there is a gap of at least two nucleotides between the 3' terminus of the primer and the variant nucleotide of the polymorphic site of the target sequence.

3. The method of claim 1, wherein said analyzing comprises determining the length of said reaction products.

4. The method of claim 1, wherein said analyzing comprises performing a technique selected from the group consisting of chromatography, capillary electrophoresis, microfluidic analysis, and slab gel electophoresis.

5. The method of claim 1, wherein said analyzing primer comprises performing high performance liquid chromatography.

6. The method of claim 1, wherein said analyzing comprises performing capillary electrophoresis.

7. The method of claim 1, wherein said analyzing primer extension products comprises determining the identity of a nucleotide incorporated in a reaction product.

8. The method of claim 1, wherein said analyzing comprises use of an intercalating agent.

9. The method of claim 8, wherein the intercalating agent is ethidium bromide.

10. Tho method of claim 8, wherein the intercalating agent is an unsymmetrical cyanin dye.

11. The method of claim 1, wherein said analyzing comprises use of slab electrophoresis and ultraviolet light.

12. The method of claim 1, wherein the reaction products are detected using slab electrophoresis and a DNA-binding dye.

13. The method of claim 1, wherein the target sequence comprises a biallelic marker associated with genetic disorders.

14. The method of claim 1, wherein the target sequence is present in a sample obtained from a diploid organism.

15. A method for screening a DNA sample for a plurality of target sequences having at least two known variants, comprising:

contacting a sample comprising a plurality of known target sequences with an extension reaction mixture to produce primer extension reaction products, the extension reaction mixture comprising

a primer that specifically hybridizes to a target sequence of interest such that there is one or more nucleotide gap between the 3' terminus of the primer and one the variant nucleotide of the polymorphic site of the target sequence, and

a mixture of deoxyribonucleoside triphosphates (dNTPs) or ribonucleoside triphosphates (rNTPs), where the dNTPs or rNTPs in the mixture provide for at least one nucleotide extension of the primer when hybridized to a target sequence having either of the two variant nucleotides, the mixture excluding a dideoxynucleoside triphosphate (ddNTP) and further excluding a dNTP or rNTP complementary to one of said variant nucleotides of the SNP, wherein the dNTPs or rNTPs in the mixture are not detectably labeled or modified; and

analyzing the primer extension products;

wherein the length of the primer extension products is indicative of the identity of the variant nucleotides at the polymorphic site.

16. The method of claim 15, wherein the target sequence is associated with genetic disorders.

17. The method of claim 15, wherein the sample is from a diploid organism.

18. The method of claim 15, wherein the extension reaction mixture comprises at least two different primers, which primers specifically hybridize to a different target sequences, wherein each primer is of a length or sequence such that extension products of the different primers can be distinguished one from another.

19. The method of claim 18, wherein the different primers are of different lengths.

* * * * *

CERTIFICATE OF FACSIMILE TRANSMISSION			
I hereby certify that this correspondence is being deposited with the United States Patent Office by facsimile transmission to the following number: 703-746-5180. **Attn: Examiner Jehanne Souaya**			
Typed or Printed Name	Martha Cisneros		
Signature		**Date**	July 2, 2003

AMENDMENT UNDER 37 C.F.R. §1.111

Address to:
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Attorney Docket No.	TGEN-001
Confirmation No.	7852
First Named Inventor	IRENA N. MERENKOVA.
Application Number	09/471,703
Filing Date	December 23, 1999
Group Art Unit	1634
Examiner Name	JEHANNE E. SOUAYA

Title: "Analysis of Nucleotide Polymorphisms at a Site"

Sir:

This amendment is responsive to the Office Action dated May 27, 2003 for which a three-month period for response was given making this response due on or before August 27, 2003. In view of the amendments to the claims and the remarks put forth below, reconsideration and allowance are respectfully requested.

AMENDMENTS

IN THE CLAIMS

1. – 68. (Canceled).

69. **(Currently Amended)** A method for determining the identity of a polymorphic nucleotide in a target sequence having at least two known variant nucleotides at a site, comprising:

performing a primer extension reaction with the target sequence using an extension reaction mixture comprising:

a primer that specifically hybridizes to the target sequence such that **there is a one or more nucleotide gap between** the 3' **terminus** ~~end~~ of the primer **and** ~~is one or more nucleotides 5' of a~~ **the** variant nucleotide **of the polymorphic site of the target sequence** ~~at the polymorphic site~~, and

a mixture of ~~a plurality of~~ deoxyribonucleoside triphosphates (dNTPs) or ribonucleoside triphosphates (rNTPs), where the ~~plurality~~ **mixture** of dNTPs or rNTPs provide**s** for at least one nucleotide extension of the primer when hybridized to a target sequence having either of the two variant nucleotides at the polymorphic site, wherein the mixture excludes a dNTP or rNTP complementary to one of said variant nucleotides of the polymorphic site, **and** wherein the dNTPs or rNTPs in the mixture are not detectably labeled or modified, and

wherein the extension reaction is performed in the absence of a dideoxynucleoside triphosphate (ddNTP); and

analyzing ~~reaction~~ **primer extension** products of said extension reaction**;**

wherein the length of the primer extension products is indicative of the identity of the variant nucleotides at the polymorphic site.

70. **(Canceled)**

71. **(Currently Amended)** The method of claim 69, wherein the primer hybridizes to the target sequence such that **there is a gap of at least two nucleotides between the 3' terminus of the primer**

and the variant nucleotide of the polymorphic of the target sequence ~~its 3' end is 2 or more nucleotides 5' of the variant nucleotide~~.

72. **(Previously Added)** The method of claim 69, wherein said analyzing comprises determining the length of said reaction products.

73. **(Previously Added)** The method of claim 69, wherein said analyzing comprises performing a technique selected from the group consisting of chromatography, capillary electrophoresis, microfluidic analysis, and slab gel electrophoresis.

74. **(Previously Added)** The method of claim 69, wherein said analyzing comprises performing high performance liquid chromatography.

75. **(Previously Added)** The method of claim 69, wherein said analyzing comprises performing capillary electrophoresis.

76. **(Previously Added)** The method of claim 69, wherein said analyzing reaction products comprises determining the identity of a nucleotide incorporated in a reaction product.

77. **(Previously Added)** The method of claim 69, wherein said analyzing comprises use of an intercalating agent.

78. **(Previously Added)** The method of claim 77, wherein the intercalating agent is ethidium bromide.

79. **(Previously Added)** The method of claim 77, wherein the intercalating agent is an unsymmetrical cyanine dye.

80. **(Previously Added)** The method of claim 69, wherein said analyzing comprises use of slab electrophoresis and ultraviolet light.

81. **(Previously Added)** The method of claim 69, wherein the reaction products are detected using slab electrophoresis and a DNA-binding dye.

82. **(Previously Added)** The method of claim 69, wherein the target sequence comprises a biallelic marker associated with genetic disorders.

83. **(Previously Added)** The method of claim 69, wherein the target sequence is present in a sample obtained from a diploid organism.

84. **(Currently Amended)** A method for screening a DNA sample for a plurality of target sequences having at least two known variants, comprising:

contacting a sample comprising a plurality of known target sequences with an extension reaction mixture **to produce primer extension reaction products**, the **extension reaction** mixture comprising

a primer that specifically hybridizes to a target sequence of interest such that **there is a one or more nucleotide gap between** the 3' ~~end~~ **terminus** of the primer **and** ~~is at least one nucleotide 5' of a~~ **the** variant nucleotide of the polymorphic site **of the target sequence**, and

a ~~plurality~~ **mixture** of deoxyribonucleoside triphosphates (dNTP**s**) or ribonucleoside triphosphates (rNTP**s**), where the ~~plurality of~~ dNTPs or rNTPs **in the mixture** provide for at least one nucleotide extension of the primer when hybridized to a target sequence having either of the two variant nucleotides, the mixture excluding a dideoxynucleoside triphosphate (ddNTP) and further excluding a dNTP or rNTP complementary to one of said variant nucleotides of the SNP, wherein the dNTPs or rNTPs in the mixture are not detectably labeled or modified; and

analyzing the ~~reaction~~ **primer extension** products ~~of each extension reaction;~~ **wherein the length of the primer extension products is indicative of the identity of the variant nucleotides at the polymorphic site**.

85. **(Previously Added)** The method of claim 84, wherein the target sequence is associated with genetic disorders.

86. **(Previously Added)** The method of claim 84, wherein the sample is from a diploid organism.

87. **(Currently Amended)** The method of claims 84, wherein the extension reaction mixture comprises **at least two** ~~a plurality of~~ different primers, which primers specifically hybridize to different target sequences, wherein each primer is of a length or sequence such that extension products of the different primers can be distinguished one from another.

88. **(Previously Added)** The method of claim 87, wherein the different primers are of different lengths.

REMARKS UNDER 37 CFR § 1.111

Formal Matters

Claims 69 and 71-88 are pending after entry of the amendments set forth herein.

Claims 69-88 were examined. Claims 69-88 were rejected. No claims were allowed.

Claims 69, 71, 84, and 87 are amended. Support for these amendments is found in the specification at, for example, page 5, line 29 to page 6, line 11. "Plurality" is amended to "mixture" simply for ease in antecedent reference in the body of the claim.

Claim 70 is canceled without prejudice.

Applicant respectfully requests reconsideration of the application in view of the amendments and remarks made herein.

No new matter has been added.

Overview of the Claimed Invention

The claimed invention is a method that provides for detection of a polymorphic nucleotide (e.g., a single nucleotide polymorphism (SNP)) in a polynucleotide in a sample, where the method involves primer extension using an extension reaction mixture comprising:

-- a primer that specifically hybridizes to a target sequence so that there is a one or more nucleotide gap between the 3' terminus of the primer and the variant nucleotide of the polymorphic site;

-- a mixture of dNTPs or rNTPs that provide for at least one nucleotide extension regardless of which of the two variant nucleotides is present at the polymorphic site

Importantly, the reaction mixture excludes:

-- a dNTP or rNTP complementary to one of said variant nucleotides

-- labeled dNTPs/rNTPs; and

-- ddNTPs.

The reaction products are then analyzed. The primers and dNTP/rNTP mixture are designed so that the length of the primer extension products is indicative of the identity of the variant nucleotides at the polymorphic site.

The method of the invention provides for certain advantages, such as:

- the cost of the method is reduced compared to conventional methods, since there is no requirement for either detectable labels or dideoxy nucleotides, which reagents are expensive
- the method provides that the dNTP/rNTP mixture and primer sequence are designed so that at least one nucleotide extension occurs regardless of which of the variant nucleotides is present at the polymorphic site so that the length of the primer extension products is indicative of the identify of the variant nucleotides at the polymorphic site.
    - the method thus provides an "internal control" for extension in that both the presence and the absence of a variant nucleotide can be detected in a single reaction – for example, if the variant nucleotide complementary to a dNTP in the mixture is absent, an extension product is formed nonetheless. Stated differently, the claimed method provides for detection of a "negative" result for a particular variant nucleotide.
    - this is in contrast to conventional methods, where the absence of the variant nucleotide complementary to a dNTP in the mixture results in no extension – one can not tell whether the extension reaction did not work or whether the variant nucleotide is not present
    - this same feature is useful in, for example, detection of whether a diploid sample is from a homozygous or heterozygous individual

We now turn to the outstanding rejections.

Interview Summary

Applicant is grateful to Examiner Souaya for her time and effort in preparation for an in-person interview with the undersigned, and her time and assistance during the interview on June 26, 2003. All outstanding rejections of the claims were discussed, and amendments and arguments proposed by counsel to distinguish the claims from the cited art and avoid the rejections under §112, ¶2 were discussed.

The Examiner and the counsel agreed upon language to avoid all rejections of the claims, which language is presented in the claim amendments submitted here.

Rejection under §112, ¶1

The claims were variously rejected as being indefinite. These rejections are addressed below.

A) Recitation of "nucleotides 5' of a variant nucleotide"

Claims 69-88 were rejected for recitation of "nucleotides 5' of a variant nucleotide". This rejection is avoided by amendment of the claims using the language kindly suggested by the Examiner. The claims now recite that the primer hybridizes to the target sequence such that there is a one or more nucleotide gap between the 3' terminus of the primer and the variant nucleotide of the polymorphic site of the target sequence. The primer thus is positioned so that the primer is extended by at least one nucleotide regardless of the identity of the variant nucleotide at the polymorphic site.

B) Recitation of "one or more nucleotides"

Claims 69-88 were rejected for recitation of "one or more nucleotides". This rejection is avoided by cancellation of claim 70 to clarify that primers that hybridize so that their 3' terminus are immediately adjacent to the variant nucleotide are excluded.

C) Recitation of "3' end"

Claims 69-88 were rejection for recitation of "3' end" of the primer. The claims are amended to recite "3' terminus" as kindly suggested by the Examiner.

In view of the above, withdrawal of the rejections of the claims under §112, ¶2 is requested.

Rejections under §103

The claims were variously rejected as being obvious under §103. These rejections are as follows:

1) Claims 69-74, 76, and 82-83 were rejected over Soderlund (EP 0648280) in view of Hoogendoorn and Kuppuswamy;
2) Claims 75 and 77-81 were rejected over Soderlund in view of Hoogendoorn and Kuppuswamy and further in view of Gibson; and
3) Claims 81, 82 and 84-88 were rejected over Soderlund in view of Hoogendoorn and Kuppuswamy and further in view of Krook

Thus in each rejection, Soderlund is cited as the primary reference.

In short, applicant respectfully submits that none of the references, either alone or combined, teach or suggest a method involving a primer extension reaction where 1) both ddNTPs and labeled dNTPs are omitted from the extension reaction; 2) the primer that specifically hybridizes to a

target sequence so that there is a one or more nucleotide gap between the 3' terminus of the primer and the variant nucleotide of the polymorphic site; and 3) the length of the primer extension products is indicative of the identity of the variant nucleotide at the polymorphic site.

We first discuss each of the references cited, and then consider the combined disclosure as applied to the claims.

Soderlund

Soderlund is cited for its disclosure of a method for detecting polymorphic nucleotides, particularly at Example 9 and in Fig. 1d. However, neither Example 9 nor any part of Fig. 1 – or any other portion of the Soderlund reference – teaches or suggests a method of that detection of the presence/absence of a variant nucleotide of a polymorphic site **without using 1) either a detectably labeled dNTP to detect primer extension (Kuppuswamy) OR 2) ddNTPs to terminate the reaction should a particular variant nucleotide be present in the target sequence (Hoogendoorn).**

Specifically, in Example 9, Soderlund indicates that the extension reaction is performed with dTTP in the reaction mix (see page 17, lines 8-11). In Fig. 1, either the dNTP is labeled or a ddNTP is present. Moreover, the primer is Fig. 1 hybridizes so that the 3' terminus is immediately adjacent the variant nucleotide, and complementary nucleotides were added to confirm the presence of the polymorphic variants.

The Office Action points to Soderlund at page 7, line 1 in support of the assertion that Soderlund teaches the use of ddNTPs is not required, and is an optional variation. However, the Office Action has not noted the context in which this statement is made. The relevant sentence from Soderlund states;

> **When a labeled dNTP is used**, it is advantageous, but not necessary, to add unlablelled ddNTPs corresponding to the other three nucleotide residues (option c in Fig 1).

(Soderlund, paragraph 57, page 7, lines 13-15, emphasis added).
From this statement in its entirety, it is evident that Soderlund only suggests that ddNTPs are optional when the dNTP is labeled. There is no teaching or suggestion that both the dNTP can be unlabeled and ddNTPs omitted as per the present claims.

With respect to the primer, the claimed method recites that the primer specifically hybridizes to a target sequence so that there is a one or more nucleotide gap between the 3' terminus of the primer and

the variant nucleotide of the polymorphic site. Soderlund states that such a primer may be used. However, in this context Soderlund also states:

> The detection primers can also be complementary to a sequence beginning several nucleotides removed from the variable nucleotide. The only limitation concerning the position of the detection step primers is that the sequence between the 3' end of the detection step primer and the variable nucleotide to be detected **must not contain a nucleotide residue of the same type as the one to be detected**.

(Soderlund, paragraph 23, page 3, line 57 to page 4, line 3, emphasis added). The claimed method avoids this technical challenge of Soderlund. Instead, the claimed method provides for the use of primers and dNTP (or rNTP) mixture so that extension products of different lengths are produced depending upon the identity of the variant nucleotide at the polymorphic site. Thus, the length of the primer extension products produced according to the claimed method is indicative of the identity of the variant nucleotides at the polymorphic site.

Hoogendoorn and Kuppuswamy

The disclosures of Kuppuswamy and Hoogendoorn have been discussed previously. The disclosure of these references with respect to the claimed method can be summarized as follows:

1) Kuppuswamy uses detectably labeled dNTPs, and is either silent as to the use of ddNTPs or does not require ddNTPs in view of the use of the labeled dNTPs
2) Kuppuswamy teaches that separate reactions should be performed for each variant nucleotide, and thus does not contemplate the design of the primer and dNTP mixture so that the identity of the variant nucleotides of the polymorphic site based upon the length of the extension products; and
2) Hoogendoorn requires the use of ddNTPs, and the length-based detection method of Hoogendoorn simply would not be operable without such ddNTPs.

Neither Kuppuswamy nor Hoogendoorn, either taken alone or in combination, suggest that detection of the presence/absence of a variant nucleotide of a polymorphic site can be detected **without using 1) either a detectably labeled dNTP to detect primer extension (Kuppuswamy) OR 2) ddNTPs to terminate the reaction should a particular variant nucleotide be present in the target sequence (Hoogendoorn)**. The claimed method explicitly excludes the use of labeled dNTPs and ddNTPs. Furthermore, in contrast to the claimed method, neither Kuppuswamy nor Hoogendoorn

provides for the use of primers and dNTP (or rNTP) mixture so that extension products of different lengths are produced depending upon the identity of the variant nucleotide at the polymorphic site.

Gibson

Gibson is cited for its disclosure of separation of DNA fragment according to size using capillary electrophoresis. Gibson adds nothing to the disclosure of the Soderlund, Kuppuswamy, or Hoogendoorn with respect to performing primer extension in the absence of labeled dNTPs and the absence of ddNTPs, or to the use of primers and dNTP (or rNTP) mixture so that extension products of different lengths are produced depending upon the identity of the variant nucleotide at the polymorphic site.

Krook

Krook is cited for its disclosure of multiplexed or polled single nucleotide primer extension reactions using more than one primer for extension, where the primers are of different lengths. Krook teaches use of a labeled dNTP in the extension reaction. Krook thus does not cure the deficiencies of the disclosures of Soderlund, Kuppuswamy, or Hoogendoorn with respect to performing primer extension in the absence of labeled dNTPs and the absence of ddNTPs, or to the use of primers and dNTP (or rNTP) mixture so that extension products of different lengths are produced depending upon the identity of the variant nucleotide at the polymorphic site..

Combined disclosures

None of the cited art, either taken alone or in any combination, teaches:

- both the dNTP can be unlabeled and ddNTPs omitted from the reaction mixture as per the present claims.
- the 3' terminus of the primer is one or more nucleotides 3' of the variant nucleotide of the target sequence
- the use of primers and dNTP (or rNTP) mixture so that extension products of different lengths are produced depending upon the identity of the variant nucleotide at the polymorphic site.

Therefore, in view of the above, the claims are not obvious in view of any combination of the cited references, and this rejection can be withdrawn.

Conclusion

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number TGEN-001.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: July 2, 2003

By: _____
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